

**Notice of Allowability**

Application No.

10/511,756

Applicant(s)

BERGMANN ET AL.

Examiner

Art Unit

Kagnew H. Gebreyesus

1656

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 8/6/07.
2. ☒ The allowed claim(s) is/are 18,19,21-24 and 26-31.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some\* c) ☐ None of the:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |  |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application  |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date <u>11/09/2007</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date _____    | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment  |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance                           |
|  | 9. <input type="checkbox"/> Other _____  |

### **DETAILED ACTION**

Applicant's response on August 06, 2007 to the Office Action dated February 05, 2007 is acknowledged. Applicants have cancelled claims 1-17. New claims 18-31 have been added. and are present for examination.

#### ***Withdrawn - Claim Rejections - 35 USC § 101***

Claims 1-17 were rejected under 35 U.S.C. 101 because the claimed recitation of a use or a method, without setting forth any steps involved in the process, results in an improper definition of a process. This rejection is withdrawn following cancellation of the claims.

#### ***Withdrawn - Claim Rejections - 35 USC § 112***

Claims 1-17 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection has been withdrawn following cancellation of claims 1-17. The rejections do not apply to the new claims.

Claim 14 was rejected for writing abbreviations at the first occurrence. This rejection is withdrawn.

Claim 10 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is withdrawn following the cancellation of the claim.

#### ***Withdrawn - Claim Rejections - 35 USC § 112***

Claims 1-16 as applied to claims 18-31 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is withdrawn following Applicant's cancellation of claims 1-17 as they apply to claims 18-31.

***Withdrawn -Claim Rejections - 35 USC § 102***

Claims 1, 4, 7 and 11 as they apply to claim 18 and 20 were rejected under 35 U.S.C. 102(b) as being anticipated by Ozaki et al. (Enzyme-Linked Immunosorbent Assay of Carbamoyl phosphate Synthase 1: Plasma Enzyme in Rat Experimental Hepatitis and Clearance. Enzyme protein 1994 95:48:213-221). This rejection has been withdrawn upon consideration of Applicants argument and claim amendments.

Claims 7, 11, 12 and 13 as applied to claims 18, 20, 25 and 26 were rejected under 35 U.S.C. 102(b) as being anticipated by Tabuchi et al (Regulation of Genes for inducible Nitric Oxide Synthase and Urea Cycle Enzymes in Rat Liver in Endotoxin Shock). Tabuchi et al disclose measuring the amount of CPS1 protein as well as mRNA and protein of other urea cycle enzymes in LPS-treated rats at 24 hrs. The reference makes the conclusion that LPS does not affect protein but affects mRNA levels of CPS1 over a 24-hour period, no data is provided beyond 24 hrs. Applicants have amended the claims to recite a method of diagnosing sepsis in humans based on increased level of human CPS1 protein using immunoassay therefore Tabuchi et al do not anticipate claims 18 and 20 thus the rejection is withdrawn.

Claim 17 was rejected under 35 U.S.C. 102(b) as being anticipated by Cerdan et al. (Role of calcium as an inhibitor of carbamoyl phosphate synthetase I). Claim 17 has

been cancelled therefore the rejection is moot.

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Charles E. Bell on November 09, 2007.

Replace claim 18 (b) with:

"determining the presence and amount of human carbamoyl phosphate synthetase 1 (CPS 1) (SEQ ID NO: 6) in said sample using an immunodiagnostic assay".

Replace claim 19(a) with:

"human CPS 1 (SEQ ID NO:6) having an apparent molecular weight of 200 kDa +/- 50 kDa using gel filtration and HPLC;

Replace claim 19(b) with:

"fragments of human CPS 1 (SEQ ID NO:6) having an apparent molecular weight of 68 to 70 kDa +/- 3kDa ; and isoelectric points in the

range from 5.5 to 6.1 in said sample using two-dimensional gel electrophoresis,

Cancel claim 20.

In claim 21, replace:

"The method of claim 20..." with "The method of claim 18..."

Cancel claim 25.

### **REASONS FOR ALLOWANCE**

The following is an examiner's statement of reasons for allowance:

The closest prior art teachings to the invention in the instant application are by Tabuchi et al and Ardawi et al. Tabuchi et al teach that rats treated with LPS (bacterial endotoxin thus mimicking sepsis) show a decrease in CPS1 mRNA at 12 hrs followed by a slight increase at 24hrs. (see fig. 2A.) However Tabuchi et al show that CPS1 protein levels are unaffected at 24 hours and no data is shown after 24hrs (see fig.3).

Ardawi et al teach that in septic rats, carbamoyl phosphate synthetase activity in the rat liver is increased by 16.4% (see table 4). However Ardawi et al (1992) does not teach or suggest increased amount of CPS1 protein in septic rats or use of an immunodiagnostic method. Furthermore Ardawi et al's study is directed to hepatic glutamine metabolism in septic rat, thus the activity of the carbamoyl phosphate synthetase measured can be that of the cytoplasmic isoform of carbamoyl phosphate synthetase; (CPS2), which is known to be involved in processing glutamine in the urea cycle. On the other hand, CPS1 is involved in processing ammonia and bicarbonate to

Art Unit: 1656

produce carbamoyl phosphate and is the rate limiting enzyme in the urea cycle. Thus at the time of the instant invention, the art was ambiguous with regards to CPS1 levels in sepsis conditions. This is because the more recent studies by Tabuchi et al (2000) that teach that there was no increase in CPS1 in rats treated with LPS (lipopolysaccharide) for at least 24 hrs.

The amended claims are drawn to a method of diagnosing sepsis in humans based on CPS1 levels using an immunodiagnostic assay thus are not anticipated.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

**Conclusion:** With the above amendments, claims 18, 19, 21-24, and 26-31 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnaw H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30 am-5: 30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nashed/  
Nashaat T. Nashed, Ph.D.  
Primary Examiner  
Art Unit 1656

Kagnew Gebreyesus PhD.  
November 09, 2007  
KHG